Claims

1. An antibody or an antigen-binding fragment thereof that binds specifically and with high affinity to both glycosylated and non-glycosylated human IL13, does not bind mouse IL13, and neutralizes human IL13 activity at an approximate molar ratio of 1:2 (MAb:IL13).

2. The antibody of claim 1, wherein the antibody is 228B/C and produced by the hybridoma designated PTA-5657.

3. An antibody that binds to the same epitope as the antibody of claim 2.

4. The antibody of claim 1, wherein the antibody is 228A-4 and produced by the hybridoma designated PTA-5656.

5. The antibody of claim 1, wherein the antibody is 227-26 and produced by the hybridoma designated PTA-5654.

6. The antibody of claim 1, wherein the antibody is 227-43 and produced by the hybridoma designated PTA-5655.

7. An antibody, wherein the antibody comprises antigen binding regions derived from the light and heavy chain variable regions of an antibody of claim 1.

8. The antibody of claim 7, wherein said antibody has a VL sequence at least 95% homologous to that set forth in SEQ ID NO: 3, and a VH sequence at least 95% homologous to that set forth in SEQ ID NO: 4.

9. The antibody of claim 7, wherein said antibody has a VL sequence at least 95% homologous to that set forth in SEQ ID NO: 5, and a VH sequence at least 95% homologous to that set forth in SEQ ID NO: 6.

10. The antibody of claim 7, wherein said antibody has a VL sequence at least 95% homologous to that set forth in SEQ ID NO: 7, and a VH sequence at least 95% homologous to that set forth in SEQ ID NO: 8.

11. A hybridoma cell line that produces a monoclonal antibody selected from the group consisting of 228B/C-1, 228A-4, 227-26, and 227-43 and designated with the ATCC deposit number PTA-5657, PTA-5656, PTA-5654, and PTA-5655, respectively.

12. A cell line comprising a nucleic acid encoding the antibody of claim 1.

13. A vector comprising a nucleic acid encoding the antibody of claim 1.

14. The antibody of claim 1, wherein the antibody is a monoclonal antibody.

15. The antibody of claim 14, wherein the monoclonal antibody is a human antibody, a chimeric antibody, or a humanized antibody.

16. A composition comprising the antibody of claim 1 and a physiologically acceptable carrier, diluent, excipient, or stabilizer.

17. A variable light chain region comprising an amino acid sequence having the formula: FRL1-CDRL1-FRL2-CDRL2-FRL3-CDRL3-FRL4, wherein FRL1 consists of any one of SEQ ID Nos: 20-25; CDRL1 consists of any one of SEQ ID NOs: 99-103; FRL2 consists of SEQ ID NO: 29; CDRL2 consists of any one of SEQ ID Nos: 104-114; FRL3 consists of any one of

SEQ ID NOs: 30-56; CDRL3 consists of any of SEQ ID NOs: 115-116; and FRL4 consists of SEQ ID NO: 57-59.

18. A variable light chain region comprising any one of SEQ ID NOs: 3, 5, 7, 93, 95, 97, 142, 144, and 150.

19. The variable light chain region of claim 17, further comprising a constant region.

20. The variable light chain region of claim 18, further comprising a constant region.

21. A variable heavy chain region comprising an amino acid sequence having the formula: FRH1-CDRH1-FRH2-CDRH2-FRH3-CDRH3-FRH4, wherein FRH1 consists of any one of SEQ ID NOs: 60-66; CDRH1 consists of any one of SEQ ID NOs: 117-122; FRH2 consists of any one of SEQ ID NOs: 67-75; CDRH2 consists of any one of SEQ ID NOs: 123-134; FRH3 consists of any one of SEQ ID NOs: 76-90; CDRH3 consists of any of SEQ ID NOs: 135-141; and FRH4 consists of SEQ ID NO: 91-92.

22. A variable heavy chain region comprising any one of SEQ ID NOs: 4, 6, 8, 94, 96, 98, 143, 145, 146, 147, 148, and 149.

23. The variable heavy chain region of claim 21, further comprising at least the CH1 domain of a constant region.

24. The variable heavy chain region of claim 23, comprising the CH1, CH2 and CH3 domains of a constant region.

25. The variable heavy chain region of claim 24, wherein the constant region is from an IgG antibody.

26. The variable heavy chain region of claim 25, wherein the IgG antibody is an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, or an IgG4 antibody.

27. The variable heavy chain region of claim 22, further comprising at least the CH1 domain of a constant region.

28. An antibody or antigen binding fragment thereof comprising the variable light chain region of claim 17, wherein the antibody binds specifically to IL13.

29. An antibody or antigen binding fragment thereof comprising the variable heavy chain region of claim 21, wherein the antibody binds specifically to IL13.

30. The antibody of claim 28, comprising a heavy chain region of claim 21.

31. The antibody of claim 30, comprising a variable light chain region having the amino acid sequence set forth in SEQ ID NO: 142 and a variable heavy chain region having the amino acid sequence set forth in SEQ ID NO: 143.

32. The antibody of claim 30, comprising a variable light chain region having the amino acid sequence set forth in SEQ ID NO: 150 and a variable heavy chain region having the amino acid sequence set forth in SEQ ID NO: 151.

33. The antibody of claim 1, wherein the antibody is a single chain antibody having the sequence set forth in SEQ ID NO:152.

34. The antibody of claim 1, wherein the antibody is a single domain antibody.

35. The antibody of claim 1, wherein the antibody is an antigen-binding fragment.

36.   The antibody of claim 35, wherein the antigen-binding fragment is a Fab.

37.   A method of treating a subject suffering from asthmatic symptoms comprising administering an amount of an antibody according to claim 1 effective to reduce the asthmatic symptoms.

38.   The method of claim 37, wherein the antibody down-regulates the activity of IL13 in the patient.

39.   The method of claim 38, wherein the antibody reduces bronchial hyperresponsiveness in the patient.

40.   The method of claim 37, wherein the antibody reduces eosinophilia in the lungs of the subject.

41.   The method according to claim 37, wherein the antibody is administered by one or more of the routes selected from the group consisting of intravenous, intraperitoneal, inhalation, intramuscular, subcutaneous and oral.

42.   The method according to claim 41, wherein the antibody is administered by inhalation.

43.   An inhalation device that delivers to a patient a therapeutically effective amount of an antibody according to claim 1.

44.   A method for detecting interleukin-13 protein in a sample, comprising the step of: allowing the antibody of claim 30 to contact a sample; and detecting the interleukin-13 through the occurrence of immunoreaction.

45.   The method of claim 44, wherein the sample is collected from a patient.

46.   A method for diagnosing overexpression of IL13 in a subject, comprising the steps of: (a) obtaining a sample from the subject; (b) combining the sample with an antibody according to claim 1 under conditions which would allow immunoreaction with IL13; and (c) determining whether or not IL13 is overexpressed relative to a normal level of expression of IL13.

47.   A method of producing the antibody of claim 1, comprising the steps of: a) producing an immunogenic compound comprising a glycosylated IL13 moiety and an immunogenic moiety; b) preparing an injectable solution comprising said immunogenic compound in phosphate buffered saline (PBS) and an adjuvant; c) immunizing a mouse with said injectable solution by a combination of intravenous and intraperitoneal injections, d) producing a hybridoma by fusing a spleen cell from said immunized mouse with a myeloma cell; e) selecting a hybridoma producing an antibody having the characteristics of the antibody of claim 1; and f) isolating said antibody.

48.   A recombinant antibody molecule, or an IL13-binding fragment thereof, comprising: at least one antibody heavy chain, or an IL13-binding fragment thereof, comprising non-human CDRs at positions 31-35 (CDR1), 50-65 (CDR2) and 95-102 (CDR3) (Kabat numbering) from a mouse anti-IL13 antibody, wherein positions 27-30 have the amino acid Gly 26, Phe 27, Ser 28, Leu 29, Asn 30; and at least one antibody light chain, or an IL-13-binding fragment thereof, comprising non-human CDRs at positions 24-34 (CDR1), 50-56 (CDR2) and 89-97 (CDR3) from a mouse anti-IL13 antibody, and framework regions from a monoclonal antibody.

49. A DNA sequence encoding the antibody of claim 30.

50. A vector comprising the DNA sequence of claim 49.

51. A host cell comprising the vector of claim 50.

52. A method for inhibiting IgE antibody production in a patient, which comprises administrating to the patient an effective amount of an IgE antibody production inhibiting effective amount of an antibody according to claim 1.

53. The method according to claim 52, wherein the inhibition of IgE antibody production is intended to prevent bronchial asthma, to prevent allergic rhinitis, to prevent allergic dermatitis, to treat bronchial asthma, to treat allergic rhinitis, to treat urticaria, to prevent anaphylaxis, or to treat atopic dermatitis.

54. A method of treating an IL13-mediated disorder in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof according to claim 1, wherein said antibody or antigen-binding fragment thereof inhibits binding of IL13 to its receptor and inhibits one or more functions associated with binding of the interleukin to said receptor.

55. The method of claim 54, wherein the disorder is allergic asthma, non-allergic (intrinsic) asthma, allergic rhinitis, atopic dermatitis, allergic conjunctivitis, eczema, urticaria, food allergies, chronic obstructive pulmonary disease, ulcerative colitis, RSV infection, uveitis, scleroderma, or osteoporosis .

56. A method of treating an IgE-mediated disorder in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof according to - claim 1, wherein said antibody or antigen-binding fragment thereof inhibits binding of IL13 to its receptor and inhibits one or more functions associated with binding of the interleukin to said receptor.

57. A method for reducing the severity of asthma in a mammal comprising administering to the mammal a therapeutically effective amount of an anti-IL13 monoclonal antibody having at least one of the following characteristics: the; ability to bind human IL13 with a K_D between about $1X10^9$ to about $1X 10^{12}$ M; the, ability to inhibit one or more functions associated with binding of the interleukin IL13 to the IL13 receptor; and the inability of the antibody does notto bind mouse IL13.

58. The method of claim 52, wherein the anti-IL13 antibody is administered by inhalation, systemically, bolus injection, or continuous infusion.

59. The method of claim 54, wherein the anti-IL13 antibody is administered by inhalation, systemically, bolus injection, or continuous infusion.

60. A peptide consisting essentially of the amino acid sequence ESLINVSG (SEQ ID NO:18).

61. A peptide consisting essentially of the amino acid sequence YCAALESLINVS (SEQ ID NO: 19).